WHAT DO YOU KNOW ABOUT UROLITHIASIS?

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ABSTRACT

Urolithiasis is ubiquitous and is prevalent in relatively young and productive age group. With changing lifestyles and climate, its prevalence has shown a rise over decades, Urolithiasis is the condition where calculi are formed in the urinary tract. Urolithiasis is the third most common disorder of the urinary tract. The worldwide incidence of Urolithiasis is quite high and in north India more than 80% of urinary calculi are calcium oxalate stones alone or calcium oxalate mixed with calcium phosphate. Many plants all over the world have been reported for significant antiurolithiatic activity. In the present paper a complete consolidated profile is reviewed here.

KEYWORDS: Urolithiasis, antiurolithiatic activity.

INTRODUCTION

Urolithiasis is also called as urinary calculi, urinary stones, kidney stones, renal stones and renal calculi refer to growth of hard, nonmetallic mineral calcifications that form in the urinary system, primarily in the kidney or ureter and may also migrate into the lower urinary system or located anywhere in the urinary system.[1] The formation of stones in the urinary tract is mainly due to crystal nucleation, crystal aggregation, crystal retention which further result in precipitation of certain substances within urine. Thus supersaturation acts as a driving force for stone formation.[2] Another theory of stone formation was identified, which mainly occur due to an imbalance between promoter (calcium, oxalate, uric acid, inorganic phosphate etc) and inhibitors (magnesium, potassium, pyrophosphate and urinary glycoprotein etc) in the kidney.[3] It is estimated that 12% of world population experiences renal stone disease with a recurrence rate of 70-80% in male and 47-60% in female.[4]
Urinary stones are typically classified by their location or by their chemical composition (calcium-containing, struvite, uric acid, or other compounds). Renal calculi are characterised clinically by colicky pain (renal colic) as they pass down along the ureter and manifest by hematuria.\textsuperscript{[5]} Drug treatments as well as invasive or surgical procedures are available to eliminate kidney stones. Drug treatment include are antibiotics, anti-inflammatory agents, muscle relaxant, analgesic etc. Non-invasive & Invasive procedures include extracorporeal shock wave lithotripsy (ESWL), percutaneous nephrolithotomy (PNL), ureteroscopy, nephrolithotomy etc. Among these procedures, extracorporeal shock wave lithotripsy (ESWL) became the standard procedure in eliminating kidney stones.\textsuperscript{[4]}

ANATOMY AND PHYSIOLOGY

The urinary system which is also called excretory system or the genitourinary system of the body. It plays a major role in homeostasis. It consists of the following structures.\textsuperscript{[6]}

- Two kidneys, produces urine.
- Two ureters, transport the urine from the kidneys to the urinary bladder.
- One urinary bladder provides temporary storage for urine.
- One urethra, through which the urine is discharged to the exterior.\textsuperscript{[6]}

KIDNEYS

The kidneys are bean-shaped organs, one on each side of the vertebral column, behind the peritoneum and below diaphragm. It has the size of a small fist. They are held in position by, a mass of fat. A sheath of fibro elastic renal fascia encloses the kidney and the renal fat.\textsuperscript{[6]}

Kidney consists of an outer cortex (below the capsule and outside the pyramids) and inner medullary portion, consisting of pale conical shaped striations, the renal pyramids and a number of distal branches called calyces. Minor and major calyces unite to form the dilated part called renal pelvis. Urine formed in the kidney is transported to the urinary bladder through ureters.\textsuperscript{[6]}

The main functions of the kidneys are

- It maintains (a) water equilibrium (b) electrolyte balance (c) acid-base balance etc.
- Formation and secretion of urine.
- It excretes waste products in the dissolved form. This includes urea, uric acid, creatinine, bilirubin etc.
• It also excretes poisonous and foreign substances from the body. This includes toxins, drugs, heavy metals, pesticides.
• It plays an important role in the regulation of arterial blood pressure, through rennin-angiotensin mechanism.
• It stimulates the production of erythrocytes by secreting erythropoietin, the hormone responsible for controlling the rate of formation of red blood cells.[6,7]

URETERS
The ureters are tubes that propel urine from the kidneys to the urinary bladder. In the adult ureters are about 25 to 30 cm long with diameter of about 3mm. The ureter arises from renal pelvis (funnel shaped) and passes through the posterior wall of the bladder. Because of this arrangement, when the urine accumulates and the pressure in the bladder rises, the ureters are compressed and the opening is blocked. Thus, prevent the backflow of urine into the ureter. Functionally, the ureters carry the urine away from kidneys into the urinary bladder by contraction of smooth muscle layer.[6]

URINARY BLADDER
The urinary bladder is a hollow muscular organ shaped like a balloon, located in the pelvic cavity. The bladder stores urine. The maximum that it can hold is one litre. It swells into a round or oval shape when it is full with urine and gets smaller when empty. In the absence of bladder disease, it can hold up to 300 ml of urine comfortably for two to five hours. The three orifices in the bladder wall form a triangle or trigone. The upper two orifices are the openings of the ureters. The lower orifice is the point of origin of the urethra.[6] Sphincters (circular muscles) regulate the flow of urine from the bladder. The bladder itself has a muscular layer (detrusor muscle) that, when contracted, increases pressure on the bladder and create urinary flow.[8] Urination is a conscious process, generally initiated by stretch receptors in the bladder wall which signal to the brain that the bladder is full. This is felt as an urge to urinate. When urination is initiated, the sphincter relaxes and the detrusor muscle contracts, producing urinary flow.[8]

URETHRA
The endpoint of the urinary system is the urethra. The urethra is a tube starting from the neck of the urinary bladder to the exterior. Its length differs in the male and in the females. The
urethra emerges from the end of the penis in males and between the clitoris and the vagina in females.\[6\]

**EPIDEMIOLOGY OF UROLITHIASIS**

Urolithiasis is a worldwide problem. The yearly incidence of urolithiasis is estimated to be about 0.5% in North America and Europe. Urolithiasis is largely a recurrent disease with a relapse rate of 50% in 5-10 year and 75% in 20 year. It is estimated that approximately about 12% of the world population experiences urolithiasis with male-female ratio of 2:1. The peak incidence is usually observed in 2\textsuperscript{nd} to 3\textsuperscript{rd} decades of life.\[5,9\]

**KIDNEY STONE FORMATION**

A kidney stone also known as renal calculus is a crystal aggregations formed in the kidneys. Kidney stones typically leave the body by passage in the urine stream, and many stones are formed and passed without causing symptoms. If stones grow to sufficient size before passage, at least 2-3 millimetres, they can obstruction of the ureter.\[10\]

**MECHANISM OF STONE FORMATION**

- Age, Profession, Nutrition, Climate, Inheritance, Sex, Mentality, Constitutions, Race
- Abnormal renal morphology, Disturbed urine flow, Urinary tract infection, Metabolic abnormalities, Genetic factors
- Increased excretion stone forming constituents, Decreased excretion of inhibitors of crystallizations.
- Physico-chemical change in the state of supersaturation
- Abnormal crystalluria, Crystal’s aggregations, Crystal’s growth

**RISK FACTORS FOR KIDNEY STONES**

- Dehydration resulting from low fluid intake is a major factor in stone formation.
- Hypercalciuria, a condition that runs in families in which urine contains unusually large amounts of calcium; this is the most common condition found in those who form calcium stones.
- Dietary factors: High intake of animal protein, meat, sodium, sugars, fructose and high fructose corn syrup, oxalate, grapefruit juice and apple juice increase the risk of kidney stone formation.\[3,11\]
- A family history of kidney stones.
• Cystic kidney diseases, which are disorders that cause fluid-filled sacs to form on the kidneys.
• Hyperparathyroidism, a condition in which the parathyroid glands, which are four pea-sized glands located in the neck, release too much hormone, causing extra calcium in the blood.
• Renal tubular acidosis, a disease that occurs when the kidneys fail to excrete acids into the urine, which causes a person’s blood to remain too acidic.\textsuperscript{[3,11]}
• Cystinuria, a condition in which urine contains high levels of the amino acid cystine.
• Hyperoxaluria, a condition in which urine contains unusually large amounts of oxalate.
• Hyperuricosuria, a disorder of uric acid metabolism.
• Blockage of the urinary tract and urinary tract infection.\textsuperscript{[3,11]}

Certain medications which increases the risk of kidney stones includes.
• Diuretics: These drugs, helps the kidneys to remove fluid from the body.
• Calcium-based antacids.
• The protease inhibitor: This drug is used to treat HIV infection. Ex: indinavir (Crixivan).
• The anti-epileptics drugs. Ex: topiramate (Topamax).\textsuperscript{[3]}

SIGN AND SYMPTOMS
• Colicky pain: It is described as the severe or strongest pain ever experienced in the flanks, lower abdomen and groin area.
• Nausea and Vomiting- usually accompanied by severe pain.
• Fever - as a result of inflammatory processes.
• Hematuria- blood in urine.
• Pyuria- resulted from pus formation due to tissue necrosis.
• Anuria- rarely happens but due to total occlusion of the passage to the ureters.
• Oliguria: reduced urinary volume.
• Dysuria: painful urination.\textsuperscript{[3,11]}

PATHOPHYSIOLOGY OF UROLITHIASIS
There are basic two aspects in the pathogenesis of kidney stone.

a) Increased urinary excretion of stone forming substances/minerals like calcium, phosphorus, uric acid, oxalate and cysteine, can cause these to get deposit as stones.
b) Physico-chemical events occurring sequentially or concurrently that influence stone formation like pH of urine, stone matrix and protective substance in urine.

Stone formation in the urinary tract occurs due to the precipitation of substances in the urine. When the urine becomes supersaturated with one or more crystal-forming substances, a seed crystal may form through the process of nucleation.\[3,11]\n
Seed crystal gets adhere to cells on the surface of a renal papilla, can grow and aggregate into an organized mass. The agents which can modify nucleation, crystallization and aggregation, pH of the urine also play important role in stone formation.\[3,11]\n
The most common locations for deposition of stones in the urinary tract.
1. At the junction of the kidney and ureter (the ureteropelvic junction).
2. At mid ureter where it crosses over the iliac bone to enter into the pelvis or where the ureter crosses over the iliac blood vessels.
3. At the junction of the ureter and bladder.
4. In women, where the ureter passes under the uterine artery.\[12]\n
**TYPE OF URINARY CALCULI**

There are four main types of urinary calculi that differ in composition and pathogenesis. The most common type of urinary calculi is calcium stones.

1. **Calcium stones**

They are the most common type of kidney stone and occur in two major forms: calcium oxalate and calcium phosphate. They are dark brown, black, grey, or white, hard, ovoid and small (1cm in diameter) dense with a sharp granular rough surface.\[3,5]\n
[Fig 1: Calcium Stones.]

1. Hypercalciuria
(Defined as excess of calcium in urine) can be idiopathic or result from any disorder that induces even mild hypercalcemia (elevated calcium (Ca\(^{2+}\)) level).

2. Hypocitraturia

(Defined as a low amount of citrate in the urine) is associated with renal lithogenesis. Citrate act in the tubular lumen by combining with calcium to form a non-dissociable but soluble complex. Hypocitraturia could result from causes of intracellular acidosis such as renal failure potassium deficiency, distal renal tubular acidosis, chronic diarrhoeal state, and drugs such as acetazolamide.\(^{[3,5]}\)

2. Uric acid stones

Uric acid stones are made up of uric acid. They are smooth, round, yellow-orange and nearly radio graphically transparent. On cut section, they show laminated structure. A diet rich in purine substances found in animal protein such as meats, fish and shellfish, result in hyperuricosuria and hyperuricaemia and in combination with low urine volume and low urinary pH, can result in uric acid stone formation.\(^{[3,5]}\)

![Fig 2: Uric Acid Stones.](image)

**TABLE I: Salient Features of Urinary Calculi.**

<table>
<thead>
<tr>
<th>Type</th>
<th>Incidence</th>
<th>Etiology</th>
<th>Pathogenesis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Calcium stones</td>
<td>75%</td>
<td>Hypercalciuria with or without hypercalcaemia idiopathic.</td>
<td>Supersaturation of ions in urine, alkaline pH of urine, low urinary volume, oxaluria and hyperuricosuria.</td>
</tr>
<tr>
<td>2. Uric acid stones</td>
<td>6%</td>
<td>Hyperuricosuria with or without hyperuricaemia.</td>
<td>Acidic urine decreases the solubility of uric acid in urine and favours its precipitations.</td>
</tr>
<tr>
<td>4. Cystine stones</td>
<td>2%</td>
<td>Genetically determined defects</td>
<td>Cystinuria containing least soluble</td>
</tr>
<tr>
<td>5. Other types</td>
<td>&lt;2%</td>
<td>Inherited abnormalities of amino acid metabolism.</td>
<td>Xanthinuria.</td>
</tr>
</tbody>
</table>

3. **Struvite or triple or mixed stones**

They are composed of magnesium, ammonium calcium and phosphate, often called as struvite, mixed stones, or triple phosphate stone. Radiographs show struvite stones as large, gnarled and laminated. They are associated with substantial morbidity infection. They tend to be soft friable and irregular in shape.\(^3,5\)

They are formed as a result of urinary tract infection with urea spitting organisms that produces urease (proteus, klebsiella, pseudomonas). Thus, they are also known as infection-induced stones. Staghorn stone which is large, solitary stone that takes the shape of renal pelvis where it is often formed as an example of struvite stone.\(^3,5\)

![Fig 3: Struvite Stones.](image-url)

4. **Cystine stones**

Formations of cystine stones are associated with cystinuria, due to genetic disorder, in the transport of cystine and other amino acids across the cell membranes of the renal tubule and the small intestinal mucosa. The stones are greenish-yellow, smooth, flecked with shiny crystallites and are moderately radio-opaque with a rounded appearance.\(^3,5\)
5. Other types of calculi

These stones usually occur as a result of a rare hereditary condition or due to inherited abnormality of enzyme metabolism, where there is a xanthine oxidase deficiency.

Ex: Hereditary xanthinuria developing xanthenes stones.\[^{3,5}\]

**DIAGNOSIS OF UROLITHIASIS**

Diagnosis of kidney stones is made on the basis of information obtained from the medical history, physical examination, urinalysis, blood test and radiographic studies or imaging test like x-ray or computerized tomography (CT) scan.

- The medical history may include questions about family history of kidney stones, diet, GI problems and other diseases and disorders.
- Physical examination may reveal fever and tenderness on the affected side.
- Urinalysis can show whether the person has an infection or the urine contains substances that form stones.\[^{11,12}\]

**IMAGING STUDIES**

**ABDOMINAL X RAY**

An abdominal X-ray is a picture created using radiation and recorded on film or on a computer. The X-rays can show the location of stones in the kidney or urinary tract. About 90% of stones with calcium can be seen on X-ray. Cystine and uric acid stones usually are not seen.\[^{11,12}\]

**ABDOMINAL ULTRASONOGRAPHY**

Abdominal ultrasonography is an imaging procedure used to examine the internal organs of the abdomen. It has limited use in the diagnosis and management of urolithiasis. It is readily
available, quickly performed and sensitive to renal calculi, it can’t detect or visualized the ureteral stones, which are far more likely to be symptomatic than renal calculi. However, if a ureteral stone is visualized by ultrasound, the finding is considered reliable. It also gives details about the presence of hydronephrosis, refer to ureteral obstruction blocking the outflow of urine.[11,13]

**KUB RADIOGRAPHY (KIDNEY, URETER, BLADDER X-RAY)**
KUB refers to a diagnostic medical imaging technique and stands for Kidneys, Ureters and Bladder also called as plain-film radiography. X-ray beams are passed through the abdomen, producing images of the kidneys, ureters and bladder on a special type of film. KUB radiography is often used as a first step in diagnosing problems of the urinary system and is usually done in conjunction with intravenous pyelography.[11,13]

![Fig 5: KUB Radiography.](image)

**Purpose of the KUB Radiography**
- To determine the size, shape and position of the kidneys and bladder.
- To detect obvious abnormalities of the urinary system, such as kidney stones.
- To help differentiate between urologic and gastrointestinal diseases, which both produce abdominal pain.
- To locate a foreign object (e.g., that has been swallowed).
- To detect air or fluid in the space surrounding the abdominal organs (peritoneal space).
KUB is typically used to investigate gastrointestinal conditions such as a bowel obstruction and gallstones and can detect the presence of kidney stones.\textsuperscript{11,13}

**INTRAVENOUS PYELOGRAPHY (IVP)**

It has been considered the standard imaging technique for urinary tract calculi. It provides useful information about the stone (size, location, radiodensity) and its environment (calyceal anatomy, degree of obstruction), as well as the contralateral renal unit (function, anomalies). With this imaging technique, ureteral calculi can be easily distinguished from other nonurologic radiopacities.\textsuperscript{11,13}

Fig 6: Intravenous Pyelography.

**NONCONTRAST HELICAL CT SCAN**

CT scan is also called as Computerized tomography scan use a combination of x-rays and computer technology to create three-dimensional (3-D) images. A CT scan may include the injection of a special dye, called contrast medium. This imaging technique is fast and accurate, and it readily identifies all stonetypes in all locations.\textsuperscript{11}

**Other diagnostic methods**

Other investigations typically carried out include:

- Microscopic study of urine, which may show proteins, red blood cells, bacteria, cellular casts and crystals.
- Culture of a urine sample to in order to identify the infecting bacteria in urinary tract.
- Blood tests: Full blood count for the presence of a raised white cell count (Neutrophilia) suggestive of infection, a check of renal function and to look for abnormally high blood calcium blood levels (hypercalcaemia).
• Urine collection to measure daily urinary volume and to determine urine levels of calcium, proteins, phosphorus, oxalate, uric acid or cystine.\textsuperscript{[11]}

**PREVENTION OF UROLITHIASIS**

The first step in preventing kidney stones is to understand, the causes of stones to form. It should be advised to adapt several lifestyle measures which will help to prevent or delay the formation of stones. Preventive measures are as follows.

• Increase fluid intake to maintain urine output at 2-3 litres per day.
• Reduce the amount of meat and animal protein eaten.
• Reduce oxalate intake (foods rich in oxalate include chocolate, rhubarb, nuts) and urate-rich foods (ex: offal and certain fish).
• Drink regular cranberry juice: increases citrate excretion and reduces oxalate and phosphate excretion.
• Maintain calcium intake at normal levels (lowering intake increases excretion of calcium oxalate).
• Depending on the composition of the stone, medication to prevent further stone formation is sometimes given, ex: thiazide diuretics (for Ca stones), allopurinol (for uric acid stones) and calcium citrate (for oxalate stones).\textsuperscript{[11]}

**PHARMACOTHERAPY OF UROLITHIASIS**

*Pain relief*

• Pain relief is the first therapeutic step in patients with an acute stone episode.
• Non-steroidal anti-inflammatory drugs (NSAIDs), usually in the form of diclofenac indomethacin or ibuprofen, should be offered first-line for the relief of the severe pain of renal colic. NSAIDs are more effective than opioids.
• Opioids, particularly pethidine, are associated with a high rate of vomiting compared with NSAIDs. If an opioid is used, it is recommended that it is not pethidine.
• Analgesia, paracetamol is safe and effective for mild-to-moderate pain, narcotics such as codeine, morphine and meperidine (Demerol) are effective in suppressing pain, they do nothing to treat its underlying cause and they have the side effects of dependence and disorientation.\textsuperscript{[14]}

**MEDICAL EXPULSIVE THERAPY (MET)**
The use of medications in order to speed the spontaneous passage of ureteral calculi is referred to as medical expulsive therapy.

<table>
<thead>
<tr>
<th>S.NO</th>
<th>DRUG CLASS</th>
<th>DRUG NAME</th>
<th>USES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Alpha blocker</td>
<td>Tamsulosin</td>
<td>Difficult urination, ureteral stone expulsion.</td>
</tr>
<tr>
<td>2.</td>
<td>Calcium channel blockers</td>
<td>Nifedipine</td>
<td>Stone expulsion, ureteral and renal calculi.</td>
</tr>
<tr>
<td>3.</td>
<td>Alpha blocker versus Calcium channel blocker</td>
<td>Tamsulosin versus Nifedipine</td>
<td>Tamsulosin provides better stone expulsion than nifedipine</td>
</tr>
</tbody>
</table>

HERBAL FORMULATION EFFECTIVE IN UROLITHIASIS

Cystone

It is an ayurvedic herbal formulation which is composed of, shilapuspha, pasanabheda, Indian madder, umbrella's edge, prickly chaff flower, sedge, purple fleabeane, lime silicate calx and shiajit, aids in keeping the urinary tract healthy. It also maintains the composition of the urine and the integrity of the mucus in the body.[15]

Actions of cystone

- It reduces the renal calculi pain.
- It can flush the kidney stones out of the body and also prevents new ones to form.
- Prevents stone formation in the urinary tract.
- Normalizes acidic urine and relieves burning urination.
- It has anti-bacterial and anti-inflammatory properties that can help stop the recurrence of urinary tract infection.[15,16]

Patients who have kidney, liver and heart impairment should take extra precautions when taking this drug cystone does not produce any side effects as long as the right amount is taken. Neither does it have any significant drug interactions. No contraindications for the use of cystone have been reported.[15]

SURGICAL TREATMENT

1. Extracorporeal shock wave lithotripsy (SWL)

It is a noninvasive technique for the removal of kidney stones. ESWL involves the use of a lithotriptor machine to generate shock waves that pass through the person’s body to break the
kidney stone into smaller pieces to pass more readily through the urinary tract. For a stone greater than 10 mm, ESWL may not help break the stone in one treatment; instead, two or three treatments may be needed.

More than 90% of stones in adults might be suitable for SWL treatment. However, success depends on efficacy of the lithotripter and the following factors.

- Size, location (ureteral, pelvic or calyceal) and composition (hardness) of the stones.
- Patient’s habitus.
- Performance of SWL.

Each of these factors has an important influence on retreatment rate and final outcome of SWL. \[13,14\]

![Fig 7: Extracorporeal Shock Wave Lithotripsy Machine.](image)

2. **Percutaneous nephrolithotomy (PNL)**

Percutaneous nephrolithotomy (PNL) is a minimally invasive surgical procedure for removal of kidney stones. In this procedure, a wire-thin viewing instrument called a nephroscope is used to locate and remove the stone.

During the procedure, a nephroscope tube is inserted directly into the kidney through a small incision in the person’s back. The nephrostomy tube drains urine and any residual stone fragments from the kidney into a urine collection bag. \[13\]
3. **Ureterorenoscopy (ureteroscope)**

A delicate ureteral stent or thin tube is inserted through the bladder into the ureter to the kidney to provide immediate relief of an obstructed kidney. They are designed to allow urine to flow past an obstruction in the ureter. They may be retained in the ureter for days to weeks as infections resolve and as stones are dissolved or fragmented by ESWL or by some other treatment.

This technique is about 90% successful and more effective than ESWL for treating stones located in the lower ureter. \[11,13\]

**PRECLINICAL MODELS FOR STUDYING ANTIUROLITHIATIC ACTIVITY IN ANIMALS**

1. **Urolithiasis induced by oxalate calculi producing diet (CPD)**
Chow et al have shown that addition of 30% glycolic acid to the standard chow diet can lead to production of renal calculi within four weeks. Related procedure is as follows.\cite{17}

Method

- Male wistar rats weighing 180-200g are acclimatised for one week and then placed randomly into groups of ten.  
- The control diet is the standard purina laboratory chow (PLC) and the oxalate calculi-producing diet (CPD) was PLC containing 3% glycolic acid. Food and water consumption are measured during the 2\textsuperscript{nd} and 4\textsuperscript{th} week of the experiment.  
- Pooled 24 h urine samples from each group are collected.  
- Five rats of each group are placed in metabolic cages from 8 am to 8 pm and the remaining five from each group complete the 24 h collection.  
- Urine Ph is measured and acidified samples are stored at -20 C until they are analyzed.  
- At the end of the 4\textsuperscript{th} week, rats are euthanized. Their urinary tracts are examined grossly and kidneys are preserved in phosphate buffered 10\% formalin and stained with Mayer’s hemotoxylin and eosin for histological studies.  
- Kidneys, heart, femur and a section of skeletal muscle were collected from each rat for oxalate and/or glycolate determination.  
- Oxalate is determined by permanganate titration.  
- Glycolate is determined by colorimetric method using 2, 7-dihydoxynapthalene after urine and tissue homogenates are prepared.

2. Ethylene glycol (EG) induced urolithiasis

Ethylene glycol (EG) induced urolithiasis model is used to assess the antiurolithiatic activity in rats.

Method

- Wistar Albino rats of male sex weighing 150-200g were used in the study.  
- They had free access to food and water and were maintained under standard laboratory conditions with alternating light and dark cycles of 12 h each.  
- They were acclimatized to laboratory conditions for 2 days before behavioral studies.  
- Animals were divided into three groups of six animals each.  
- Group I served as normal and received regular water and food \textit{ad libitum}.  

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\textsuperscript{17} Chow et al.
- Group II served as control and was given ethylene glycol (0.75%) in drinking water for induction of kidney stones until 28th day.
- Group III received reference standard Cystone (750mg/kg) from day 15 to 28 as it served as curative regimen.
- All animals were kept in individual cages and urine sample of 24h were collected on 29th day. They had free access to drinking water during the urine collection period.
- Urine was analyzed for calcium, phosphate and oxalate content. The blood was collected through retro-orbital plexus under anaesthetic conditions and animals were sacrificed by cervical decapitation.
- Serum was separated by centrifugation at 10,000 × g for 10 min and analyzed for Creatinine, Urea and Uric Acid were estimated.
- The results were expressed as the Mean + SD and analysed using one-way ANOVA followed by Dunnett’s multiple comparison tests and Student’s “t”-test. $P < 0.05$ was considered statistically significant.\textsuperscript{18-43}
Table II: Plants with Antiurolithiatic Activity.

<table>
<thead>
<tr>
<th>SNo</th>
<th>Name of the plant &amp; Family</th>
<th>Part</th>
<th>Extract</th>
<th>Model</th>
<th>Animal</th>
<th>Parameter</th>
<th>Mechanism of action</th>
<th>Dose (mg/kg)</th>
<th>Pvalue</th>
<th>Author</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Phoenix dactylifera F: Fabaceae</td>
<td>Fruits</td>
<td>Aqueous n-butanol</td>
<td>Ethylene Glycol Induced</td>
<td>Albino Rats</td>
<td>Urine analysis, Serum analysis</td>
<td>Decrease urea and uric acid levels. Reduce the formed CaOx stones</td>
<td>EC: 075% Aqu &amp; n-butanol Extract: 200 Cystone: 750</td>
<td>&lt;0.001</td>
<td>Challa Srinivas Reddy, et.al April (2013).[19]</td>
</tr>
<tr>
<td>2</td>
<td>Megarajanga Chooranam (Siddha drug)</td>
<td>Ethylene Glycol Induced</td>
<td>Albino Rats</td>
<td>Urine analysis, Serum analysis</td>
<td>Due to Diuretic and Lithotriptic Activity</td>
<td>EC: 075% Extract: 50 &amp; 100, Cystone: 750</td>
<td>&lt;0.01</td>
<td>K. Kanakavall, et.al May (2013).[20]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Triphala karpa chooranam</td>
<td>Ethylene Glycol and Calcium Induced</td>
<td>Albino Rats</td>
<td>Urine analysis, Serum analysis</td>
<td>Possess CaOx Crystal inhibitory, diuretic, antioxidant, epithelial cell Protective</td>
<td>EC: 075% Extract: 90 Cystone: 750</td>
<td>&lt;0.01</td>
<td>A. Tamil Selvan, et.al July-Sep (2013).[21]</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Polyherbal formulation: Plectranthus mollis Didymocarpus Taraxacum officinale</td>
<td>Petroleum ether Hydroalcholic Ethyl acetate</td>
<td>Calcium oxalate Induced</td>
<td>Albino Rats</td>
<td>Urine analysis, Serum analysis, biochemical parameters</td>
<td>Decreased the quantity of CaOx deposited in the kidneys</td>
<td>Extract: 100 &amp; 200</td>
<td>&lt;0.01</td>
<td>DG. Baheti, et.al. (2013).[22]</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Dolichos biflorus F: Fabaceae</td>
<td>Seeds</td>
<td>Aqueous</td>
<td>Calcium oxalate stone by homogenous preparation</td>
<td>-</td>
<td>Percentage Dissolution of Calcium oxalate</td>
<td>Due to lithotriptic property</td>
<td></td>
<td></td>
<td>Roshini barad, et.al (2013).[23]</td>
</tr>
<tr>
<td>6</td>
<td>Cucumis sativus Fruits</td>
<td>Ethanol</td>
<td>Ethylene Rats &amp; Urine analysis,</td>
<td>Reduced</td>
<td></td>
<td></td>
<td></td>
<td>EC: 075% in</td>
<td>&lt;0.001</td>
<td>Krishnaveni,</td>
</tr>
<tr>
<td></td>
<td>Plant Family</td>
<td>Part</td>
<td>Extract Type</td>
<td>Inducer</td>
<td>Species</td>
<td>Type of Analysis</td>
<td>Excretion of Oxalate and Phosphate</td>
<td>Water Excretion</td>
<td>Authors, Year</td>
<td></td>
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<tr>
<td>7.</td>
<td>F: cucurbitaceae</td>
<td>Roots</td>
<td>Hydro alcoholic</td>
<td>Ethylene Glycol Induced</td>
<td>Albino Rats</td>
<td>Urine, Serum analysis</td>
<td>Due to diuretic and anti-inflammatory effects</td>
<td>EC: 1% in water</td>
<td>Ahmadi et al. (2012) [25]</td>
<td></td>
</tr>
<tr>
<td>8.</td>
<td>F: Malvaceae</td>
<td>Roots</td>
<td>Ethanolic</td>
<td>Ethylene Glycol &amp; Ammonium Chloride</td>
<td>Albino Rats</td>
<td>Urine, Serum analysis, Histopathology</td>
<td>Possess diuretic property, antioxidant effect &amp; protective activity</td>
<td>EC: 0.75% Extract: 200, 400, 800, 1600, NH₄Cl: 2% in water</td>
<td>Narumal Damodaram et al. (2012) [26]</td>
<td></td>
</tr>
<tr>
<td>9.</td>
<td>F: Liliaceae</td>
<td>Roots &amp; Seeds</td>
<td>Aqueous</td>
<td>Ethylene Glycol Induced</td>
<td>Albino Rats</td>
<td>Urine, Serum analysis, Kidney wt</td>
<td>Decrease kidney stones and serum levels</td>
<td>EC: 0.75% Extract: 500 &amp; 100, Furosemide: 20</td>
<td>Chandak et al. (2012) [27]</td>
<td></td>
</tr>
<tr>
<td>10.</td>
<td>F: Verbenaceae</td>
<td>Roots</td>
<td>Ethanolic</td>
<td>Ethylene Glycol Induced</td>
<td>Albino Rats</td>
<td>Urine, Serum analysis, Kidney wt</td>
<td>Exhibit antiurolithiatic activity in dose dependant manner</td>
<td>EC: 0.75% Extract: 200 Cystone: 750 Oleanolic acid: 60 &amp; 80</td>
<td>Narendra Vyas et al. (2012) [28]</td>
<td></td>
</tr>
<tr>
<td>11.</td>
<td>F: Amaranthaceae</td>
<td>Seeds</td>
<td>Ethanolic</td>
<td>Ethylene Glycol Induced</td>
<td>Albino Rats</td>
<td>Urine, Serum analysis,</td>
<td>Possess diuretic activity &amp; also prevention of crystal aggregation</td>
<td>EC: 0.75% Extract: 250 &amp; 500, Cystone: 750</td>
<td>Joshi Pranav et al. (2012) [29]</td>
<td></td>
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<tr>
<td>12.</td>
<td>F: Gentianaceae</td>
<td>Stems</td>
<td>Ethanolic</td>
<td>Ethylene Glycol</td>
<td>Albino Rats</td>
<td>Urine, Serum analysis</td>
<td>Possess diuretic activity &amp; also</td>
<td>EC: 0.75% in water</td>
<td>Parmar et al. (2012) [30]</td>
<td></td>
</tr>
</tbody>
</table>
| 13 | Hordeum vulgare  
F: Poaceae | Seeds | Ethanolic | Ethylene Glycol Induced | Albino Rats | Urine analysis, Serum analysis, Kidney analysis | Possess diuretic property, antioxidant, Nephroprotective property. | EC: 075% in Water Extract: 100, 250 & 500 | <0.05 |
| 14 | Saccharum spontaneum  
F: Poaceae | Root | Ethanolic | Glycolic acid Induced | Albino Rats | Urine analysis, Serum analysis, | Decreases the supersaturation of the urine with respect to CaOx. | Glycolic acid: 3% Extract: 200 & 300 | <0.05 |
| 15 | Polyherbal formulation:  
Hemidesmus, Zingiber officinalis, Glycyrrhiza glabra, Nelumbo, Myristic fragments | Roots Rhizome, Root, Petal, Fruits | Aqueous | Ethylene Glycol Induced | Albino Rats | Body weight, Urine analysis, Serum analysis | Reduced excretion of Calcium, oxalate and phosphate. Increased Excretion of Citrate and Magnesium. | EC: 075% in water 1g of NH₄Cl Extract: 1 & 2, Cystone: 5ml/kg | <0.00, <0.05, <0.01 |
| 16 | Benincasa Hispida  
F: cucurbitaceae | Seeds | Ethanolic | Ethylene Glycol Induced | Albino Rats | Urine analysis, Serum analysis | Increased diuresis, reduction in stone forming constituents in urine. | EC: 075% in water Extract: 250 & 500, Cystone: 750 | <0.05 |
| 17 | Ichnocarpus Frutescens  
F: Apocynaceae | Root | Ethyl acetate | Ethylene Glycol Induced | Albino Rats | Urine analysis, Serum analysis | Reduced the elevated urinary ox. | EC: 075% in water Extract: | <0.001 <0.01 <0.05 |
<table>
<thead>
<tr>
<th>No.</th>
<th>Plant Name</th>
<th>Plant Part</th>
<th>Extraction Method</th>
<th>Animal Model</th>
<th>Analysis</th>
<th>Effect</th>
<th>EC</th>
<th>Study Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>18</td>
<td>Pergularia daemia</td>
<td>Whole plant</td>
<td>Alcoholic</td>
<td>Albino Rats</td>
<td>Urine analysis, Serum analysis, Kidney analysis</td>
<td>Reduction in stone forming constituents in urine &amp; decreased kidney</td>
<td>EC: 0.75% in water, Extract: 400 Cystone: 750</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>19</td>
<td>Crataeva magna</td>
<td>Bark</td>
<td>Aqueous Ethanol</td>
<td>Albino Rats</td>
<td>Urine analysis, Serum analysis, Kidney Analysis</td>
<td>Decrease kidney stones and serum levels</td>
<td>EC: 0.75% in water, Extract: 400, NH₂Cl: 2%, 3% Lactose, Cystone: 750</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>20</td>
<td>Unex Capsule: Boerhaavia diffusa and Tribulus terrestris.</td>
<td>-</td>
<td>Aqueous</td>
<td>Albino Rats</td>
<td>Urine analysis, Serum analysis, Kidney Analysis</td>
<td>Reduced the growth of the urinary stone.</td>
<td>EC: 0.75% Unex extract: 200 &amp; 400, Cystone: 750</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>21</td>
<td>Momordica charantia</td>
<td>Fruits</td>
<td>Aqueous Alcoholic</td>
<td>Albino Rats</td>
<td>Urine analysis, Serum analysis</td>
<td>Reduction in the stone forming constituents in urine and renal tissue</td>
<td>EC: 0.75% Aqueous &amp; alcoholic extract: 200 &amp; 250</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>22</td>
<td>Solanum xanthocarpum</td>
<td>Fruits</td>
<td>Methanolic</td>
<td>Albino Rats</td>
<td>Urine analysis, Serum analysis</td>
<td>Due to CaOX Crystal inhibition, diuretic, anti-oxidant effect</td>
<td>EC: 0.75% Extract: 100, 200, Cystone: 750</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>23</td>
<td>Moringa Oleifera</td>
<td>Bark</td>
<td>Aqueous</td>
<td>Albino</td>
<td>Urine analysis,</td>
<td>Reduction in</td>
<td>EC: 0.75% in</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
CONCLUSION
The present review conveys information about urolithiasis its types, causes pathophysiology and treatment. The majority of stones are calcium based and may be asymptomatic but if they cause pain or obstruction, they must either pass out of the urinary system on their own or be removed surgically. Urolithiasis is more in those people whose diet is very rich in animal protein or who do not consume enough water or calcium.
REFERENCES

13. Andrew J. Portis, M.D. And Chandru P. Sundaram, M.D. Diagnosis and Initial Management of Kidney Stones, AFP, 2001; 67(7): 1329-1338.


